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10/736,112	12/15/2003	Jeffrey S. Ross	10448-201001 / MPI03-005P	5668

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FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/736,112	ROSS, JEFFREY S.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-40* is/are pending in the application.

4a) Of the above claim(s) *17-32 and 35-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-16,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/24/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant cancels claim 2.

Accordingly, claims 1, 3-16, 33-34 are being examined.

Withdrawn Rejection

The objection, and 112, second paragraph rejection, items 2, claim 4, and item 3, claims 33-34, have been withdrawn, in view of the amendment.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-16, 33-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons already of record in paper of 12/14/06.

The response asserts that the rejection is obviated by the amendment of claims 1 and 3, to recite "a reference standard that is statistically significant between subjects having recurrence and subjects that do not have recurrence".

The response has been considered but is not found to be persuasive for the following reasons:

It is still not clear what constitutes a reference standard.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-16, 33-34 remain rejected under 35 U.S.C. 112, first paragraph, for lack of a clear written description of PSMA, for reasons already of record in paper of 12/14/06.

The response asserts that PSMA is a known protein, with a known amino acid sequence. The response recites Capon v. Eshhar v. Dudas, 2005, asserting that the court teaches that re-description of what was already known is not required.

The response has been considered but is not found to be persuasive for the following reasons:

PSMA is reasonably interpreted as a **genus** of PSMA variants, with unknown structure and function, and not a single protein, in view of the disclosure in the specification. The specification discloses that the term "human PSMA" refers to at least two protein products, human PSMA and PSM', which have or are homologous to (e.g., at least about 85%, 90%, 95% identical to) an amino acid sequence as shown in Israeli et al. (1993) Cancer Res. 53:227-230; Su et al. (1995) Cancer Res. 55:1441- 1443; US 5,538,866, US 5,935,818, andWO 97/35616; or which is encoded by (a) a naturally occurring human PSMA nucleic acid sequence (e.g., Israeliet al. (1993) Cancer Res. 53:227-230 or US 5,538,866); (b) a nucleic acid sequence degenerate to a naturally occurring human PSMA sequence; (c) a nucleic acid sequence **homologous to (e.g., at least about 85%, 90%, 95% identical to**) the naturally occurring human PSMA nucleic acid sequence; or (d) a nucleic acid sequence that hybridizes to one of the foregoing nucleic acid

sequences under stringent conditions, e.g., highly stringent conditions (p.17). Therefore, Capon v. Eshhar v. Dudas does not apply here. Which of the PSMA is referred to is not clear, nor is it described in the specification.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 1, 3-16, 33-34 remain rejected under 35 U.S.C. 112, first paragraph, for lack of enablement of a method for determining risk of prostate cancer recurrence, by detecting an increased PSMA level of expression, for reasons already of record in paper of 12/14/06.

1. Essential material

The response asserts that PSMA is well known in the art, and one could practice the claimed invention without undue experimentation. The response asserts that as such, the amino acid sequence of PSMA is not "essential material".

The response has been considered but is not found to be persuasive for the following reasons:

PSMA is required to practice the claimed method, and thus clearly is an essential material. PSMA, however, is described in the specification only by reference to publication. MPEP 608.01 teaches that incorporation of **essential material** in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference (see 37 CRF 1.57).

2. Determination of risk of prostate cancer recurrence

The response recites a press release, 2004, by the Cytogen Corporation unrelated to the instant Applicants that discusses the data presented in the present application and states that "we believe that the publication of clinical data showing overexpression of PSMA in primary cancer ... independently predicts disease recurrence." The response recites Perner et al, 2007, which evaluate 450 patients with prostate cancer, and which using univariate and multivariate analysis of PSMA level of expression conclude that high PSMA levels are associated with significant increase in PSA recurrence.

The recitation of the press release and Perner et al is acknowledged.

The response has been considered but is not found to be persuasive for the following reasons:

Concerning the press release, it cannot be evaluated, since there is no data accompanying the press release.

Concerning Perner et al, although Pernier et al show a correlation between PSMA level and PSA recurrence, Perner et al assert the predictive value of PSMA based solely on univariate and multivariate analysis of PSMA level of prostate cancer patients. However, whether such data could be used for predicting risk of recurrence in an unknown population of treated patients, who are in remission, is **not predictable**, in view that, similar to the instant application, there is **no validation** of the data against a prospective population trials. Such validation is necessary, in view that:

1) The teaching in the art is **contradictory** concerning whether PSMA level is predictive of recurrence of prostate cancer. For example, Bostwick et al, 1998, of record, also using

statistical analysis (p.2258, first column, third paragraph), teach that PSMA level is not predictive of recurrence of prostate cancer. The teaching of Bostwick et al is confirmed by Beckett et al, 1999, and Thomas et al, 2002, all of record. On the other hand, Rosenthal et al, 2001, and Murphy et al, 1998, teach that PSMA level is predictive of recurrence of prostate cancer.

2) In a similar situation with the marker hsp27 as predictive of breast cancer, where there are contradicting results, even with univariate analysis, Oesterrich et al, of record, confirm the need to perform validation studies (p.1205, first column, para before last).

3) Tockman et al, of record, teach that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and **confirm marker predictive value in prospective population trials** (emphasis added) (see abstract).

The response asserts that it is not clear the relevance of the teaching of Oesterreich et al.

The response has been considered but is not found to be persuasive for the following reasons:

The teaching of Oesterreich et al is relevant to the instant application, because correlation of a marker with its prognostic value, when based solely on statistical analysis, needs validation, as taught by Oesterreich et al, in view that false positive correlation does occur. This false positive correlation is also confirmed in another presumably prognosis maker, Id2, in view of the teaching of Vandersompele et al, of record.

The response asserts that the Tockman et al. and Vandesompele et al. references, related to a different kind of marker -one for early detection of primary cancers--is not relevant to the predictability of the claimed method, which is for recurrence of prostate cancer.

The response has been considered but is not found to be persuasive for the following reasons:

The need for validation of a maker for its predictive value in a prospective population trial, as taught by Tockman, applies as well to the instant application, especially in view of contradictory results in the art, concerning the predictive value of PSMA.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-6, 11-16 remain rejected under 35 U.S.C. 102(b) as being anticipated by Murphy et al, 1998 (Urology, 51: 89-97), for reasons already of record in paper of 12/14/06.

The response asserts that Murphy et al do not teach or suggest that at any particular stage of the disease there can be statistically significant variation between the patients at that stage to assess the risk of recurrence in a subset of the patients.

The response has been considered but is not found to be persuasive for the following reasons:

Murphy et al teach standard errors for PSMA data in remission patients, which are well into the ranges of 0.02 or 0.03 (table V, on page 94), and thus are clearly statistically significant.

New Rejection based on the Amendment

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-16, 33-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-16, 33-34 are indefinite, for the use of the language "statistically significant", which is a relative term.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SHANON FOLEY can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
September 02, 2007

/Larry R. Helms/

Supervisory Patent Examiner